CME

Obsessive–Compulsive Disorder and Related Conditions

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Childhood onset of obsessive–compulsive disorder (OCD) is not uncommon, so the pediatrician needs to be familiar with its presentation and comorbidity. It is a neuropsychiatric disorder with genetic vulnerabilities and environmental risk factors. Children with early onset of OCD are at increased risk for tic disorder and attention-deficit hyperactivity disorder (ADHD). A particular subtype characterized by abrupt onset subsequent to Group A beta-hemolytic streptococcal (GABHS) infection may be mediated by an autoimmune process. Identification of subtypes may lead to the delineation of risk factors and interventions. Practice parameters recommend the serotonin reuptake inhibitors and cognitive–behavioral therapy with response prevention as treatments. Children with streptococcal-precipitated OCD may merit a different assessment and treatment.

EDUCATIONAL OBJECTIVES

1. Identify the common presenting symptoms of obsessive–compulsive disorder (OCD) in children and adolescents.
2. Discuss the appropriate medication treatments currently available for children with OCD.
3. Review the current psychotherapeutic treatments used for children with OCD.

PHENOMENOLOGY

Childhood-onset OCD is a common, chronic, and often undiagnosed disorder with significant morbidity. Epidemiologic studies estimate that 1 in 200 children and adolescents have OCD, and that only one-fourth of them have received professional evaluation and treatment.[1] Among adults with OCD, at least one-third to half had their illness as children or adolescents. A variety of factors have led to the underdiagnosis of the illness, ranging from patients' feeling humiliated and needing to hide their symptoms to the lack of access to effective treatments in many areas.

OCD is defined by having recurrent obsessions, compulsions, or both that cause marked distress or interfere with one's life.[2] These obsessions are recurrent and persistent thoughts, images, or impulses that are distressing and intrusive. The compulsions are repetitive, purposeful behaviors performed in response to an obsession to neutralize it and alleviate the worry. The symptoms must be distressing, must be time consuming (more than 1 hour per day), or must significantly interfere with function to meet criteria for the disorder.[2] The requirement that the individual must recognize his or her thoughts or actions as excessive or unreasonable is waived for children. Frequently, young children perform the behaviors without being able to explain specifically why they must or why the actions are senseless.[3]

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Interestingly, there is a finite list of obsessions and compulsions. This lends credence to the hypotheses about the ethologic explanations for the symptoms.[3,4] Many of the obsessive symptoms can be understood as excessive worries about danger, separation, and contamination, which result in rituals of compulsive washing, checking, and hoarding. These have parallel "hardwired" behaviors in the animal world, suggesting a possible origin for OCD. The most common obsessions include excessive concerns about contamination (eg, dirt, germs, or illness), harm coming to self or others, doing the right thing (scrupulosity), reassurance, or sexual thoughts. Sometimes a need ("urge") for evenness, order, or exactness may be described with an accompanying feeling of "incompleteness." The most common rituals are washing, repeating, checking, counting, touching, arranging, and hoarding.[3]

Children have obsessions and compulsions comparable to those of adults, except that they are more age appropriate (eg, children worry that they might be kidnapped or that their parents might be killed).[3] It is not unusual for OCD symptoms to change over time, and most children will experience most of the symptoms at some time during the course of their illness.[3]

Boys are more likely to have prepubertal onset and girls are more likely to have pubertal onset of OCD. The male-to-female ratio equalizes in adolescence.[3] In general, children with early-onset OCD seem to have a higher rate of comorbid ADHD, tic disorders, or both. For those with OCD, ADHD, and tic disorder, the onset of the tic disorder may precede OCD by several years.[3] It is hypothesized that early-onset OCD may represent a unique subtype of this disorder. Evidence suggests that children who have early-onset OCD prior to 9 years of age have a higher rate of first-degree relatives with OCD or a tic disorder, and thus have greater "genetic loading" than those with later-onset OCD.[5]

The differential diagnosis is broad and includes anxiety and depressive disorders with obsessional features. Additionally, stereotypies and the "rigid behavior" in Asperger's syndrome and other developmental disorders may resemble OCD. Tic disorders, anxiety disorders, disruptive behavior disorders, and learning disorders are common comorbid diagnoses.[3] There is a high comorbidity between OCD and tic disorders,[3,5] and a child who presents with OCD should be carefully assessed for this. Usually, a ritual can be distinguished from a tic, although on occasion the premonitory or sensory tic resembles a ritual.[6]

ETIOLOGY

OCD is often cited as the classic neuropsychiatric disorder, with neurotransmitter dysregulation, genetic vulnerabilities, and environmental moderators clearly implicated in its pathogenesis. Basal ganglia disorders with OCD symptomatology and brain imaging studies have led to hypotheses about the relevant circuitry (frontal lobe–limbic–basal ganglia).[7] Family studies suggest that OCD and Tourette's syndrome may in some cases represent alternate expressions of the same gene(s). However, there are cases without familial vulnerability.[5]

Recently, post-streptococcal autoimmunity has been postulated as another potential cause of some childhood-onset OCD.[8] This was based on findings from two parallel lines of research: investigations of childhood-onset OCD and Tourette's syndrome and a study of Sydenham's chorea, the neurologic variant of rheumatic fever. Sydenham's chorea is believed to develop due to cross-reaction of anti-GABHS antibodies with neurons in the central nervous system.[9] Several reports have noted the development of obsessive-compulsive symptoms with Sydenham's chorea, and that these symptoms resolve as the chorea disappears.[10,11]

In a study of children with OCD, an abrupt onset or exacerbation of symptoms was noted subsequent to GABHS infection. These children with streptococcal-precipitated OCD or tics also had an abrupt onset of symptoms and a dramatic course characterized by severe exacerbations. Further study revealed that this subgroup was distinguished by prepubertal onset of symptoms, frequent neurologic abnormalities, and an episodic course in which symptom exacerbations were abrupt, dramatic, and precipitated by GABHS infections. The children are thought to mount a postinfectious systemic immunologic response to GABHS. The exact nature of this response is not completely understood, but it

may affect neuronal function in the basal ganglia in children who are genetically susceptible.[8] This work led to the description of a distinct subgroup of children with early-onset OCD or tic disorders believed to be precipitated by GABHS infection. This subgroup is described by the following working criteria: (1) presence of OCD or a tic disorder; (2) onset of symptoms at puberty; (3) episodic course of severity of symptoms; (4) association with GABHS infection; and (5) association with neurologic abnormalities.[8] The underlying hypothesis is that autoimmunity mediates the neuropsychiatric symptoms. Hence, the group has been called pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS).[12]

There are several reports of streptococcal-precipitated OCD or tic disorders. Kiessling et al.[13] found a temporal relationship between GABHS infection and the abrupt onset of tics in some of their patients. Others have reported movement disorders, other than chorea, after GABHS infection.[14,15]

EVALUATION AND ASSESSMENT

There are two guidelines for the assessment of children and adolescents with OCD—The Expert Consensus Guideline Series on the Treatment of OCD[16] and the American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameters for the Assessment and Treatment of Children and Adolescents with OCD.[17] Both present detailed reviews of the literature and expert advice on a broad range of practical clinical issues. Detailed information about onset (abrupt versus insidious), course (waxing and waning versus episodic), and comorbidity assists in identifying subtypes.

In combination with a clinical interview, rating scales such as the Children's Yale-Brown Obsessive Compulsive Scale[18] are frequently used. Part of that scale, the Children's Yale-Brown Obsessive Compulsive Scale Symptom Checklist, is particularly useful in a clinical interview to elicit specific symptoms. It is relatively easy to administer, and can also be used to measure the severity of symptoms and their change over time.

A child presenting with an acute onset or dramatic, unexplained clinical exacerbation of OCD, with or without tics, requires a thorough assessment of recent medical illnesses, including seemingly benign upper respiratory tract infections.[16,17] The pediatrician should ask about any bacterial or viral illnesses in the past several months, as well as whether there is a family history of rheumatic fever or Sydenham's chorea. A throat culture, high or rising antistreptolysin O, antistreptococcal DNaseB titers, or all three may aid in determining whether symptoms were precipitated by GABHS infection.[17]

TREATMENT

Selection of Treatment(s)

Planning treatment for children and adolescents with OCD requires consideration of both the OCD diagnosis and comorbidity plus psychosocial factors. The Expert Consensus Guideline[16] and the AACAP Practice Parameters[17] note that only cognitive-behavioral therapy, specifically the technique of exposure with response prevention, and pharmacologic treatment with serotonin reuptake inhibitors have systematic evidence of efficacy. However, other types of individual and family psychotherapy may play an important role in the overall treatment plan for these children and adolescents.

No clear empirical data exist to inform the pediatrician about whether to begin with cognitive-behavioral therapy, medication, or both. The AACAP Practice Parameters favor cognitive-behavioral therapy as the initial treatment for younger children and for children and adolescents with milder symptoms without significant comorbidity. Cognitive-behavioral therapy has the advantages of apparent durability and avoidance of risks associated with medication. Sometimes, a serotonin reuptake inhibitor or a selective serotonin reuptake inhibitor (SSRI) may be the initial treatment method due to urgency, expense, lack of trained clinicians, insufficient cognitive ability to participate in cognitive-behavioral therapy, or lack of family support.

Cognitive-Behavioral Therapy

In general, cognitive-behavioral therapy is the psychotherapeutic treatment of choice for children and adolescents with OCD. Although the lit-

erature increasingly supports using cognitive–behavioral therapy as the first-line treatment for children and adolescents, the systematic studies lag behind those done in adults.[14,17]

The specific technique of exposure with response prevention is the intervention of choice for cognitive–behavioral therapy. The child is exposed to the feared situation and then the response (eg, ritual or avoidance behavior) is prevented until anxiety decreases. By combining exposure with response prevention, the patient learns that the feared consequences do not take place and the resultant anxiety diminishes. The systematic exposure results in the habituation of anxiety and then the correction of mistaken cognitions that, in turn, reduce OCD symptoms.[19,20]

Although there are no large, well-controlled pediatric studies of cognitive–behavioral therapy, pilot studies exist. In general, studies of cognitive–behavioral therapy have yielded impressive responses (with symptom rating scores decreasing by 50% to 65%), although many were complicated by subjects' taking concurrent medication. Piacentini provides a review of cognitive–behavioral therapy for pediatric OCD.[19] The best known cognitive–behavioral therapy protocol is detailed by March and Mulle.[20] Unfortunately, despite its applicability in most cases, behavioral therapy is frequently not implemented for OCD.

Providing cognitive–behavioral therapy for OCD requires specialized training in cognitive–behavioral principles and in exposure with response prevention techniques. In most cases, the depth of this training and the intensity of the treatment regimen (eg, requiring weekly or twice weekly office visits) make it impractical for pediatricians to direct treatment from their offices. Rather, referral to a psychologist or another mental health professional with behavioral or cognitive–behavioral training is usually warranted.

Psychopharmacotherapy

Increasing evidence supports the efficacy of serotonin reuptake inhibitors and SSRIs in children with OCD. Clomipramine, a tricylic antidepressant with serotonin reuptake inhibition, was studied first in the pediatric population and has been approved by the Food and Drug Administration for the treatment of OCD in children 10 years and older.[21,22] In one study, despite improvements in symptoms, more than 80% of participants continued to meet criteria for the clinical diagnosis of OCD at follow-up.[23]

Clomipramine is generally well tolerated by pediatric patients. Side effects are primarily secondary to its anticholinergic and antihistaminic activities and these are comparable to (but milder than) those seen in adults.[21,22] Electrocardiograms for concerns about tachycardia and prolongation of the QTc interval should be obtained in ongoing clinical care.[24]

Recently, the SSRIs have become available and have been popular due to fewer antihistaminic and anticholinergic side effects. Monitoring of electrocardiograms is not required, and SSRIs are much safer in overdose than are the tricyclic antidepressants. The side effect profile includes sedation, nausea, diarrhea, insomnia, anorexia, tremor, sexual dysfunction, and hyperstimulation.[25,26] Large, multicenter, controlled trials of sertraline and fluvoxamine have been completed. Both medications appear to be effective with 30% to 40% symptom reduction, which is similar to the effectiveness of clomipramine.[25,26] The Food and Drug Administration has approved fluvoxamine for the treatment of children 8 years and older and sertraline for children as young as 6 years. Studies of paroxetine and fluoxetine for OCD in children are ongoing.

A substantial minority of patients will not respond until after 8 or even 12 weeks of pharmacotherapy.[21] Thus, it is important to wait at least 8 weeks, and preferably 10 weeks, before changing agents, adopting high dosage strategies, or undertaking augmentation regimens.[16] Approximately one-third of patients may fail to respond to monotherapy with a given serotonin reuptake inhibitor,[7] and the likelihood of responding decreases considerably after a third trial of serotonin reuptake inhibitor.[16]

How long should patients who respond to medication continue to take it? Periodic discontinuation (or lowering of dose) is generally advisable, and many clinicians use 6 months of subclinical symptoms as a time to consider such action.[16] The literature suggests that many responders experience a relapse when medication is discontinued.[27] A lowering of dosage may help identify the mini-

mal dose required to maintain symptom relief. Generally, the medication is not stopped abruptly due to concerns about discontinuation syndromes and the return of OCD symptoms.

Combined Treatment

In clinical practice, pharmacotherapy and cognitive–behavioral therapy work well together. Many believe that children with OCD require, or benefit more from, combined treatments. Unfortunately, no large, controlled studies have been published comparing cognitive–behavioral therapy, medication, or their combination in children and adolescents. However, such investigations are ongoing. Intuitively, one would expect combined therapy to have an advantage over monotherapy with medication, but this cannot be concluded until controlled trials are completed.

Augmentation Strategies

Reports suggest that 40% to 60% of adults with OCD show partial or no response to an adequate trial of a serotonin reuptake inhibitor[26] and that many others experience a return of symptoms when medication is discontinued. The Practice Parameters recommended that cognitive–behavioral therapy augment medication, and this is the best strategy.[16] Sometimes children require a focused psychosocial intervention, rather than a second medication, so it is important to distinguish psychosocial from pharmacologic targets when considering additional treatments.

Various strategies for augmentation of medication have been studied in adults who were considered nonresponders or partial responders, although few such trials have examined this systemically. One augmentation strategy added medications that enhance serotonin function (eg, lithium, buspirone, and clonazepam) to a serotonin reuptake inhibitor. Overall, results have been disappointing. In the treatment of adults with refractory symptoms, lithium and buspirone were not effective as augmenting agents for a serotonin reuptake inhibitor in controlled trials.[28]

The other augmentation strategy, and the one best studied, is the addition of a low-dose dopamine antagonist. Augmentation of a serotonin reuptake inhibitor with pimozide or haloperidol has been effective for decreasing OCD symptoms in controlled trials.[28] The development of the atypical dopamine antagonists (eg, risperidone, which is a 5-HT2A/D2 antagonist) has made newer agents with less risk for acute and long-term extrapyramidal side effects available. McDougle et al.[28] reported that augmentation of a serotonin reuptake inhibitor with risperidone was significantly superior to placebo in reducing the OCD symptoms of adults with treatment-refractory illness.

However, limited data exist supporting medication augmentation for children and adolescents who have symptoms that are refractory to treatment with serotonin reuptake inhibitors. Children and adolescents appear to have response and relapse rates to serotonin reuptake inhibitors that are generally similar to those of adults. A rare case of augmentation of a serotonin reuptake inhibitor with clonazepam has been cited, but concerns about disinhibition, tolerance, and dependence limit its use.[29] Rare reports indicate that clomipramine has been added to an SSRI with varying results, but concerns remain about drug–drug interaction (with some of the SSRIs' inhibiting the metabolism of clomipramine) plus the increased risk of adverse events such as serotonin syndrome, tachycardia, and cardiac conduction delays.[24,30] Thus, a combination of clomipramine and an SSRI would be reserved for only the most severe cases and would require monitoring of electrocardiograms and blood levels.

As in the adult literature, pediatric research has focused on the dopamine antagonists, specifically risperidone. Fitzgerald et al.[31] described a series of four pediatric patients whose conditions significantly improved after risperidone was added to their serotonin reuptake inhibitor therapy. These children have continued taking this combination. Two of the four patients achieved "near-total remission" with the addition of risperidone. The authors conclude that augmentation of serotonin reuptake inhibitor therapy with risperidone may improve the response of pediatric patients with OCD. Large-scale, double-blind, placebo-controlled studies of this combination are warranted in both pediatric and adult patients with OCD.

The most common side effects of risperidone

include sedation, restlessness, increased appetite, weight gain, and dry mouth.[28,31] Extrapyramidal effects are rare. Although the risk of tardive dyskinesia is significantly less for an atypical dopamine antagonist, it remains a rare possibility and it must be weighed in the risk–benefit ratio. Weight gain can be problematic during risperidone therapy, and monitoring of weight is recommended. There are rare cases of hepatotoxicity, and this may be related to weight gain associated with steatohepatitis.[32] It is difficult to estimate this risk, and liver function tests are not typically monitored in the community for patients taking risperidone.[32] Increased prolactin levels have been reported with risperidone therapy, although prolactin is not routinely monitored in the community.[33]

Investigational Treatments

The children who meet criteria for PANDAS may merit different treatment considerations. Of course, a documented positive result for GABHS infection on throat culture would be treated with appropriate antibiotics, as per the community standard. Without a positive result on throat culture, antibiotics are not indicated.

Hypotheses concerning whether Sydenham's chorea and PANDAS might have similarities in their pathophysiology have led to the question of whether penicillin prophylaxis would reduce the exacerbation of neuropsychiatric symptoms in children with PANDAS by preventing streptococcal infections. An 8-month, double-blind, placebo-controlled, crossover trial of oral penicillin V (250 mg twice a day) and placebo has been conducted in 37 children.[34] There was no significant difference between phases in the severity of either OCD or tics. The oral penicillin failed to provide adequate prophylaxis against or elimination of GABHS infection, as evidenced by the fact that 14 of 35 GABHS infections were detected during the penicillin phase. Several children received antibiotic treatment multiple times during the placebo phase.

The study does not provide justification for penicillin prophylaxis in the ongoing care of children with PANDAS.[34] The authors found that because of the failure to achieve an acceptable level of streptococcal prophylaxis, no conclusions could be drawn regarding the efficacy of penicillin prophylaxis in preventing exacerbation of tics or OCD symptoms.[34] Studies that employ a more effective prophylactic agent and include a larger sample size are needed.

If post-streptococcal autoimmunity is the cause of the exacerbations in this subgroup, children with PANDAS might benefit from immunomodulatory therapies that have been shown, preliminarily, to treat the symptoms of Sydenham's chorea.[35] Children with severe, infection-triggered exacerbations of OCD or tic disorders were randomly assigned to plasma exchange (5 single-volume exchanges during 2 weeks), intravenous immunoglobulin (1 g/kg/d on 2 consecutive days), or placebo (saline solution given in the same manner as intravenous immunoglobulin).[36] Plasma exchange and intravenous immunoglobulin were both effective in lessening the severity of symptoms in this group of children. Ratings were completed at 1 month, and symptom gains were maintained at 1 year.[36] These children had more significant impairment than the average child with OCD or tics, and this was why these invasive interventions were considered. Currently, these interventions are investigational and should be considered only in the context of research approved by a human investigation committee and not in the context of routine clinical care. This issue is reviewed elsewhere.[37]

CONCLUSION

The search to identify subtypes of childhood-onset OCD may lead to better delineation of risk factors and, thereby, potential interventions. The PANDAS subtype is particularly interesting, as novel prophylactic and therapeutic strategies may be identified. Given the severity, chronicity, and resulting impairment, it is critical to identify the illness early in its course and to develop new treatments.

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